TRANS-ATLANTIC DEBATE

Thomas L. Forbes, MD, and Jean-Baptiste Ricco, MD, PhD, Section Editors

Asymptomatic carotid artery stenosis—Medical therapy alone versus medical therapy plus carotid endarterectomy or stenting

Peter A. Schneider, MD[a] and **A. Ross Naylor, MD,**[b] *Honolulu, Hawaii; and Leicester, United Kingdom*

Vascular surgery has matured to the point that there exists robust bodies of literature exploring many of our therapies. However, this evidence is but one of the factors that dictate medical practice. Others include local patient demographics, the practical implications of healthcare delivery, and an individual surgeon's interpretation of this evidence, which can be somewhat subjective. As a result, there are numerous examples of vascular specialists' practice patterns differing depending on their geographic location. Recognizing this, the Editors of the *Journal of Vascular Surgery* and the European Journal of Vascular and Endovascular Surgery have developed a series of Trans-Atlantic Debates to explore these instances. The inaugural debate explores the controversial question of how best to manage asymptomatic carotid artery stenoses. Our debators, Peter Schneider and Ross Naylor, offer reasoned and passionate arguments to defend their differing approaches. We trust that this addition to our journals will prove enlightening and, perhaps, entertaining. (J Vasc Surg 2010;52:499-507.)

PART I: CAROTID ENDARTERECTOMY OR STENTING IN ADDITION TO MEDICAL THERAPY IS STILL THE BEST WAY TO TREAT MOST ASYMPTOMATIC PATIENTS WITH 60% TO 99% CAROTID STENOSIS.

—Dr Peter A. Schneider

Repair of carotid stenosis, in addition to best medical therapy (BMT), is currently the best way to treat most asymptomatic patients with 60% to 99% carotid stenosis. Carotid stenosis causes preventable strokes. The unfortunates who present with stroke due to carotid stenosis (and their even more unfortunate counterparts who experienced a fatal stroke as the first sign of trouble) all harbored an asymptomatic lesion before their respective events. Carotid repair used judiciously in concert with BMT and performed well can have life-long protective effects against stroke-related death and disability for patients with asymptomatic carotid stenosis.[1-3]

There is a difference between critical analysis and being unreasonably critical. Reckless claims have been made about the superiority of BMT alone for 60% to 99% carotid stenosis.[4-7] Small patient cohorts that have included minor lesions with limited follow-up have done "well" with BMT alone and that has been used to advocate the cessation of carotid repair.[8-13] Practitioners have been accused of self-enrichment as the motivation for carotid repair.[14] We are proudly informed that in the United Kingdom, only 20% of patients undergoing CEA are being treated for asymptomatic carotid stenosis, while many times that number who could benefit from repair will go on to have preventable stroke.[14,15]

This leads to the following points:

1. Each time repair plus BMT has been compared with BMT alone, repair has had significant and lasting benefits.[1-3] There are numerous current organizational guidelines recommending repair and detailing the benefits (Table I).[16-19]
2. Anyone who believes that they are performing carotid repair for their own benefit and not for the benefit of the patient should stop doing it immediately.[14]
3. BMT has produced stroke reduction in a variety of populations but has not been well tested among good-risk patients with significant asymptomatic carotid stenosis who would otherwise be candidates for repair.[5,8,9,20-24]

From the Division of Vascular Therapy, Kaiser Foundation Hospital, Honolulu[a]; and the Department of Vascular Surgery, Leicester Royal Infirmary, Leicester.[b]

Competition of interest: none.

This article is being co-published in the *Journal of Vascular Surgery*® and the *European Journal of Vascular and Endovascular Surgery.*

Correspondence: Peter A. Schneider, MD, Division of Vascular Therapy, Kaiser Foundation Hospital, 3288 Moanalua Rd, Honolulu, HI 96819 (e-mail: Peter.Schneider@kp.org); and Prof A. Ross Naylor, Vascular Surgery Group, Division of Cardiovascular Sciences, Robert Kilpatrick Clinical Sciences Bldg, Leicester Royal Infirmary, LE2 7LX Leicester, UK (e-mail: ross.naylor@uhl-tr.nhs.uk).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/$36.00

doi:10.1016/j.jvs.2010.05.063

Table I. Guidelines from various organizations for repair of asymptomatic carotid stenosis

Organization	*Year*	*Guideline*
American Academy of Neurology	2005	Stenosis 60% to 99%. CEA can reduce future stroke rate if the perioperative complication rate is kept low.[16]
American Heart Association	1998	Stenosis 60% to 99%. CEA indicated when it can be performed with less than 3% stroke and death rate.[17]
European Society of Vascular Surgery	2009	CEA recommended in asymptomatic men with <75 years of age with 70% to 99% stenosis, if the perioperative stroke and death rate is <3%. CEA should be considered in younger, fit women.[18]
Society for Vascular Surgery	2008	Stenosis 60% to 99%, CEA plus BMT, if the perioperative risk is low.[19]

Table II. Perioperative risk of carotid endarterectomy in patients with asymptomatic carotid stenosis

Source	*Year*	*Patients (N)*	*Stroke (%)*	*Death (%)*	*Stroke/death (%)*
ACAS[2]	1995	724	. . .	. . .	2.3
ACST[1]	2004	1348	. . .	. . .	2.8
US National Inpatient Sample[25]	2008	111,684	0.88	0.38	. . .
Northern New England Vascular Group[26]	2008	1732	. . .	. . .	1.4
NSQIP[27]	2009	5009	0.96	0.56	1.7

ACAS, Asymptomatic Carotid Atherosclerosis Study; *ACST,* Asymptomatic Carotid Surgery Trial; *NSQIP,* National Surgical Quality Improvement Program.

4. Repair has also improved due to patching and medical management and has been performed with lower risk than before (Table II).[1,2,25-28] Antiplatelet agents and statins have made repair as much as 50% safer.[26,29-32] The small long-term annual risk of ipsilateral stroke of about 0.5% in repair patients may be even smaller when BMT is optimized.
5. Current research will help guide therapy by identifying those most likely to benefit from repair in addition to BMT and those who are at high risk for repair and therefore, less likely to benefit.[7,10,11,13,26,33,34]
6. Consideration should be given to a randomized trial of BMT alone vs BMT plus repair, but this will likely take a decade to plan and conduct.

WHAT IS THE EVIDENCE FOR REPAIR (IN ADDITION TO MEDICAL MANAGEMENT)?

After a significant carotid stenosis has developed, that lesion remains a threat to the patient until it is removed. In the Asymptomatic Carotid Surgery Trial (ACST), for example, the annual risk of stroke after repair (0.55%) was much less than the annual risk with BMT alone (1.9%).[1] The Asymptomatic Carotid Atherosclerosis Study (ACAS) and ACST studies both compared carotid endarterectomy (CEA) plus BMT vs BMT alone, and both studies demonstrated a decreased risk of stroke by approximately 50% at 5 years, even though both studies were biased against repair.[1,2]

The risk of repair is front-loaded and the downside is evident ≤30 days. BMT is "pay-as-you-go," and the risks only become evident over time. The risk of BMT alone is subject to underestimation if there is loss to follow-up, death of undetermined cause, small patient cohorts, or crossover to repair. ACAS and ACST both grossly underestimated the long-term benefits of repair for some of these reasons and by curtailing follow-up soon after the benefit of repair had been determined. Had patients been monitored longer, the benefit of repair would likely have been greater because the annual risk of stroke after repair was much less than the annual risk with BMT alone.[3] To put it another way, any patient who lived more than a couple years experienced a benefit to carotid repair every year for the rest of their lives, while every patient who did not undergo repair continued to face an excess annual threat. In addition, it is possible that contemporary BMT, which was not fully implemented during ACST (70% were taking statins by conclusion of the trial), would further decrease the small annual risk of stroke after repair. We will learn more about this from the Carotid Revascularization Endarterectomy vs Stent Trial (CREST).[35]

Repair plus BMT was shown to be the better treatment in ACST, even though the study was biased against CEA. Only 91% of patients randomized to repair received it, and 18% of those randomized to BMT underwent repair. Technique and perioperative management were not standardized. Had all CEA patients been taking statins and antiplatelet agents and received a patch at surgery, risk would likely have been lower.[28,29,32] Contemporary results of CEA show improvement and are in the range of 1.5% stroke/death risk (Table II). The perioperative risk of stroke and death for CEA in asymptomatic patients in CREST was low and will serve as a benchmark.[35]

CAS is a maturing procedure, has improved significantly over the past several years, and will likely continue to improve as we better understand appropriate patient selection. Data available for CAS in asymptomatic patients outside of CREST comes from high-risk registries. For example, among 516 asymptomatic patients with high-risk anatomy for CEA, the perioperative stroke/death rate for CAS was 1.8%.[36] The Asymptomatic Carotid Trial-1 study

is continuing to enroll standard-risk asymptomatic patients randomized to BMT plus CEA or CAS. In the lead-in phase, the stroke/death rate for CAS was 1.3%, with no ipsilateral strokes between 30 days and 1 year.[37] Alternative methods of cerebral protection, such as reversed flow, may also play a role.[38-40]

Effort has been devoted to understand which patients are most likely to benefit from repair. This will decrease the number needed to treat to prevent a stroke. High-risk groups are being identified, including those with silent infarcts, certain plaque characteristics, microemboli on transcranial Doppler (TCD) imaging, rapid plaque progression, and others.[7,10,12,13,34,41]

The bottom line: BMT plus repair was much better than BMT alone, even in a level I study biased against repair. BMT has improved, but other things have changed as well. As long as the perioperative risk of repair remains about the same as or less than the risk of BMT alone at 2 years, it will continue to benefit good-risk patients to consider repair in addition to BMT.

WHAT IS THE EVIDENCE FOR BMT ALONE?

We have no level I data showing that BMT alone in any era has been better than BMT plus repair. We don't know if the risk of BMT alone is low enough to obviate the benefits of repair. Shouldn't we know the answer to that before we abandon the patients who could benefit from repair? The assertion that BMT has solved the problem of asymptomatic carotid stenosis comes from several recent studies: SMART, Oxford Vascular, Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) study, and studies by Spence and Abbott.[7-9,11,12] These studies are not adequate to determine care.

The SMART study, an often-cited source for the supremacy of BMT, monitored 221 patients with questionnaires.[8] Many of these patients would not be considered for repair because a peak systolic velocity (PSV) of only 150 cm/s was required to be included. Only 96 patients had a 70% to 99% stenosis, with a PSV >210 cm/s. Stroke occurred in 2.7% over 3.6 years, but 6% had CEA and 1% had CAS. Deaths due to stroke were included in the general category of death (15%), and we don't know how many deaths were stroke-related. The Oxford Vascular Study reported a 0.34% ipsilateral stroke rate per year with BMT alone.[9] Ipsilateral transient ischemic attacks developed in another 1.8%, and many participants went on to have CEA. Other territory strokes occurred in 8.3% per year. Unspecified vascular death occurred in 7.7%. The study monitored 101 patients with >50% stenosis, but only 32 had 70% to 99% stenosis. Three of these 32 had a stroke during follow-up.

In another line of investigation, Spence et al[7] used TCD to identify asymptomatic carotid stenosis patients (PSV >170 cm/s) with and without microemboli.[7] Those with microemboli had a stroke risk of 10.3% the first year and 18.5% the second year. One can only guess why all the microemboli patients were not referred for CEA after the first year. In those who did not have microemboli, the first-year risk of stroke was 1.4% and the second-year risk of stroke was 1.8%. Although Spence et al advocate against repair in this group (those remaining after the high-risk microemboli patients are excluded), the cumulative 2-year risk of stroke was approximately 3.2% with contemporary BMT alone. This is only a little less than the 2-year stroke risk in the all-comers BMT group in the ACST (about 4%) and is more than twice as high as the perioperative risk of CEA plus BMT in the CREST study.[35] When other end points were included (stroke or death or CEA) in those with no microemboli, the risk was 6.5% at 2 years. Even in the lower-risk group with no microemboli, the benefit of repair in addition to BMT could be significant if repair is provided at a low risk, in the range of ≤2%.

In another study, Abbott et al[12] did not show such a dramatic difference between those with and without microemboli on TCD. The annual transient ischemic attack (TIA)/stroke risk was 10% in the microemboli group and 7% in the group with no microemboli. These groups both would likely benefit from repair as long as it can be done with low risk. ACSRS monitored 462 patients who had >60% stenosis in relationship to bulb diameter by the ECST method (these could be 30% diameter reduction by North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria). CT scans were performed to identify those with silent cerebral infarcts. The ipsilateral annual event rate was 4.6% when infarcts were present and 2.4% when no infarcts were present. The annual risk of stroke was 3.6% with and 1% without silent infarcts.[10]

These mentioned studies have been used to extrapolate a trend and suggest a stroke rate that approaches zero with modern BMT.[4] This is duly noted but is indirect evidence of the benefits of BMT. These studies were generally compromised by a number of recurring problems: inclusion of minimal lesions, unclear end points, mixed groups, short-term follow-up, and only small groups with bona fide carotid stenosis that would have been considered for repair. In each of the aforementioned studies, for example, duplex imaging was used to quantify carotid stenosis. The last time that a major asymptomatic carotid study carefully analyzed degree of stenosis by angiography was in the follow-up of NASCET patients with asymptomatic contralateral carotid stenosis.[42] The stroke rate was 3.2% per year, and the highest risk was in those with 75% to 94% stenosis (18.5% stroke at 5 years). Incidentally, 80% of the strokes were not preceded by TIA. Calls for the cessation of repair are being made on the basis of these data, without much acknowledgment of the challenges of BMT alone.

BMT is desirable and necessary and is discussed as if it were fully formed and possible to broadly implement. In fact, BMT is not simple to characterize or to produce. It is challenging to accomplish in broad populations because it is expensive, time-consuming, complicated, requires vigilance and compliance, and has its own side effects and complications.[43] There are those who will not be able to quit smoking and those who cannot tolerate statins or antiplatelet agents. Not everyone will be convinced to take

flax seed and grapefruit juice. Today's BMT will be tomorrow's obsolete practice.

What is the real-world risk of stroke with BMT alone, especially over the long-term, given that there will be noncompliance and intolerance that reduce the efficacy of the medical regimen? Compliance with a complex medical regimen will likely be higher in a study where investigators go about proving biases with impractical labor-intensive practices but likely lower in the real world. Whereas in the real world, you have either had your carotid fixed or not. In addition to the disadvantages of BMT, there is a downside to lack of repair: continued annual risk of stroke in excess of the annual risk after repair, psychologic effects of living with a threatening lesion, and the potential of long-term cognitive deterioration.[44-48]

Drawing ridiculous conclusions from skimpy evidence, some have called for a cessation or severe limitation of carotid repair.[4,5,49] It is disingenuous to treat small groups of asymptomatic patients with nonlesions, see that they remain asymptomatic with BMT, and then claim victory. The old risks of repair are being compared with pseudonatural history studies of modern BMT in patients with lesions that might never have been considered for repair. All the while, those with carotid stenosis could go on to have preventable strokes without repair under a misguided and nihilistic approach. Incidentally, what is the late follow-up of medically managed patients who still harbor these lesions? We don't have any.

CONCLUSION

Patients that present with stroke due to carotid stenosis, at some previous time, had an asymptomatic lesion and an opportunity for repair. Repair of carotid stenosis, by CEA and in some cases CAS, in addition to BMT, is currently the best way to treat most asymptomatic patients with 60% to 99% carotid stenosis. How well can BMT alone handle the problem? This will take a trial and 10 years. What we know now is that each time it was fairly evaluated, when repair was added to BMT, it cut the risk in half. When repair is used judiciously in concert with BMT and performed well, it can have life-long protective effects against stroke-related death and disability for patients with asymptomatic carotid stenosis. We should continue to provide repair to good-risk patients with significant asymptomatic carotid stenosis and continue to look for ways to identify which patients are most likely to benefit from repair.

REFERENCES

1. MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomized controlled trial. Lancet 2004;363:1491-502.
2. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-8.
3. Chambers BR, Donnan G. Carotid endarterectomy for asymptomatic carotid stenosis. The Cochrane Library 2008;4:1-20.
4. Abbott AL. Medical (nonsurgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. Stroke 2009;40:e573-83.
5. Spence JD. Asymptomatic carotid stenosis: criterion standard should be medical therapy. Arch Surg 2009;144:382-3.
6. Abbott AL, Bladin CF, Levi CR, Chambers BR. What should we do with asymptomatic carotid stenosis? Int J Stroke 2007;2:27-39.
7. Spence JD, Coates V, Li H, Tamayo A, Munoz C, Hackam DG, et al. Effects of intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis. Arch Neurol 2010;67:180-6.
8. Goessens BM, Visseren FL, Kappelle LJ, Algra A, van der Graaf Y. Asymptomatic carotid artery stenosis and the risk of new vascular events in patients with manifest arterial disease: the SMART study. Stroke 2007;38:1470-5.
9. Marquardt L, Geraghty OC, Mehta Z, Rothwell PM. Low risk of ipsilateral stroke in patients with asymptomatic carotid stenosis on the best medical treatment. A prospective, population-based study. Stroke 2010;41:e11-7.
10. Kakkos SK, Sabetai M, Tegos T, Stevens J, Dafydd T, Griffin M, et al. Silent embolic infarcts on computed tomography brain scans and the risk of ipsilateral hemispheric events in patients with asymptomatic internal carotid artery stenosis. J Vasc Surg 2009;49:902-9.
11. Nicolaides AN, Kakkos SK, Griffin M, Sabetai M, Dhanjil S, Tegos T, et al. Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) Study Group. Severity of asymptomatic carotid stenosis and risk of ipsilateral hemispheric ischaemic events: results from the ACSRS study. Eur J Vasc Endovasc Surg 2005;30:275-84.
12. Abbott AL, Chambers BR, Stork JL, Levi CF, Donnan GA. Embolic signals and prediction of ipsilateral stroke or transient ischemic attack in asymptomatic carotid stenosis: a multicenter, prospective cohort study. Stroke 2005;36:1128-33.
13. Spence JD, Tamayo A, Lownie SP, Ng WP, Ferguson GG. Absence of microemboli on transcranial Doppler identifies low-risk patients with asymptomatic carotid stenosis. Stroke 2005;36:2373-8.
14. Naylor AR, Gaines PA, Rothwell PM. Who benefits from intervention for asymptomatic carotid stenosis: patients or professionals? Eur J Vasc Endovasc Surg 2009;37:625-32.
15. Great Britain and Ireland Carotid Endarterectomy Audit 2008. http://www.vascularsociety.org.uk.
16. Chaturvedi S, Bruno A, Feasby T, Holloway R, Benavente O, Cohen SN, et al. Carotid endarterectomy-an evidence-based review. Report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. Neurology 2005;65:794-801.
17. Biller J, Feinberg WM, Castaldo JE, Whittemore AD, Harbaugh RE, Dempsey RJ, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke 1998;29:554-62.
18. Liapis CD, Bell PR, Mikhailidis D, Sivenius J, Nicolaides A, Fernandes e Fernandes G, et al. ESVS guideline Collaborators. ESVS Guidelines. Invasive treatment for carotid stenosis: Indications, techniques. Eur J Vasc Endovasc Surg 2009;37(4 suppl):1-19.
19. Hobson RW 2nd, Mackey WC, Ascher E, Murad MH, Calligaro KD, Comerota AJ, et al. Management of atherosclerotic carotid artery disease: clinical practice guidelines of the Society for Vascular Surgery. J Vasc Surg 2008;48:480-6.
20. Sillesen H, Amarenco P, Hennerici MG, Callahan A, Goldstein LB, Zivin J, et al on behalf of the SPARCL Investigators. Atorvastatin reduces the risk of cardiovascular events in patients with carotid atherosclerosis. A secondary analysis of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Trial. Stroke 2008;39:3297-302.
21. Sillesen H. What does best medical therapy really mean? Eur J Vasc Endovasc Surg 2008;35:139-44.
22. Heart Protection Study Collaborative Group. Effects of cholesterol lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high risk conditions. Lancet 2004;363:757-67.
23. Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomized trials of anti-platelet therapy for prevention of death, myocardial infarction and stroke in high risk patients. BMJ 2002;324:71-86.
24. Bhatt DL, Fox KA, Hacke W, Berger PB, Black HR, Boden WE, et al. for the CHARISMA Investigators. Clopidogrel and aspirin versus aspi-

rin alone for the prevention of atherothrombotic events. N Engl J Med 2006;354:1706-17.
25. McPhee JT, Schanzer A, Messina LM, Eslami MH. Carotid artery stenting has increased rates of postprocedure stroke, death, and resource utilization than does carotid endarterectomy in the United States, 2005. J Vasc Surg 2008;48:1442-50.
26. Goodney PP, Likosky DS, Cronenwett JL, for the Vascular Study Group of Northern New England. Factors associated with stroke or death after carotid endarterectomy in Northern New England. J Vasc Surg 2008;48:1139-45.
27. Kang JL, Chung TK, Lancaster RT, LaMuraglia GM, Conrad MF, Cambria RP. Outcomes after carotid endarterectomy: is there a high risk population? A National Surgical Quality Improvement Program report. J Vasc Surg 2009;49:331-9.
28. Rerkasem K, Rothwell PM. Patch angioplasty versus primary closure for carotid endarterectomy. The Cochrane Library 2009:CD000160.
29. Payne DA, Jones CI, Hayes PD, Thompson MM, London NJ, Bell PR, et al. Beneficial effects of clopidogrel combined with aspirin in reducing cerebral emboli in patients undergoing carotid endarterectomy. Circulation 2004;109:1476-81.
30. Molloy KJ, Thompson MM, Schwalbe EC, Bell PR, Naylor AR, Loftus IM. Comparison of levels of matrix metalloproteinases, tissue inhibitor of metalloproteinases, interleukins, and tissue necrosis factor in carotid endarterectomy specimens from patients on versus not on statins preoperatively. Am J Cardiol 2004;94:144-6.
31. Perler BA. The effect of statin medications on perioperative and long-term outcomes following carotid endarterectomy or stenting. Semin Vasc Surg 2007;20:252-8.
32. Brooke BS, McGirt MJ, Woodworth GF, Chang DC, Roseborough GS, Freischlag JA, et al. Preoperative statin and diuretic use influence the presentation of patients undergoing carotid endarterectomy: results of a large single-institution case-control study. J Vasc Surg 2007;45:298-303.
33. Kadoglou NP, Sailer N, Moumtzouoglou A, Kapelouzou A, Gerasimidis T, Liapis CD. Aggressive lipid lowering is more effective than moderate lipid lowering in carotid plaque stabilization. J Vasc Surg 2010;51:114-21.
34. Kadoglou NP, Gerasimidis T, Moumtzouoglou A, Kapelouzou A, Sailer N, Fotiadis G, et al. Intensive lipid-lowering therapy ameliorates novel calcification markers and GSM score in patients with carotid stenosis. Eur J Vasc Endovasc Surg 2008;35:661-8.
35. CREST Executive Committee. Carotid Revascularization Endarterectomy Versus Stenting Trial. Presented at: Annual Stroke Association International Stroke Conference 2010, San Antonio, Texas, Feb 24-26, 2010.
36. Massop D, Dave R, Metzger C, Bachinsky W, Solis M, Shah R, et al; on Behalf of the SAPPHIRE Worldwide Investigators. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHIRE Worldwide Registry First 2001 patients. Catheter Cardiovasc Interv 2009;73:129-36.
37. Stroke Trials Registry. The lead-in results for ACT 1 trial. www.strokecenter.org/trials/trialdetail.aspx.
38. Criado E, Fontcuberta J, Orgaz A, Flores A, Doblas M. Transcervical carotid stenting with carotid artery flow reversal: 3-year follow-up of 103 stents. J Vasc Surg 2007;46:864-9.
39. Alvarez B, Ribo M, Maeso J, Quintana M, Alvarez-Sabin J, Matas M. Transcervical carotid stenting with flow reversal is safe in octogenarians: a preliminary safety study. J Vasc Surg 2008;47:96-100.
40. Kelso R, Clair DG. Flow reversal for cerebral protection in carotid artery stenting: a review. Perspect Vasc Surg Endovasc Ther 2008;20:282-90.
41. Sabeti S, Schlager O, Exner M, Mlekusch W, Amighi J, Dick P, et al. Progression of carotid stenosis detected by duplex ultrasonography predicts adverse outcomes in cardiovascular high-risk patients. Stroke 2007;38:2887-94.
42. Inzitari D, Eliasziw M, Gates P, Sharpe BL, Chan RKT, Meldrum H, et al; for the North American Symptomatic Carotid Endarterectomy Trial Collaborators. The causes and risk of stroke in patients with asymptomatic internal carotid stenosis. N Engl J Med 2000;342:1693-700.
43. Mitka M. Improving medication adherence promises great payback, but poses tough challenge. JAMA 2010;303:825.
44. Fukunaga S, Okada Y, Inoue T, Hattori F, Hirata K. Neuropsychological changes in patients with carotid stenosis after carotid endarterectomy. Eur Neurol 2006;55:145-50.
45. Landgraff NC, Whitney SL, Rubinstein EN, Yonas H. Cognitive and physical performance in patients with asymptomatic carotid artery disease. J Neurol 2010 [Epub ahead of print: doi: 10.1007/s00415-009-5449-z].
46. Landgraff NC, Whitney SL, Rubinstein EN, Yonas H. Use of the physical performance test to assess preclinical disability in subjects with asymptomatic carotid artery disease. Phys Ther 2006;86:541-8.
47. Johnston SC, O'Meara ES, Manolio TA, Lefkowitz D, O'Leary DH, Goldstein S, et al. Cognitive impairment and decline are associated with carotid artery disease in patients without clinically evident cerebrovascular disease. Ann Intern Med 2004;140:237-47.
48. Romero JR, Beiser A, Seshadri S, Benjamin EJ, Polak JF, Vasan RS, et al. Carotid artery atherosclerosis, MRI indices of brain ischemia, aging, and cognitive impairment: the Framingham study. Stroke 2009;40:1590-6.
49. Abbott A. Asymptomatic carotid artery stenosis: it's time to stop operating. Nat Clin Pract Neurol 2008;4:4-5.

Submitted May 12, 2010; accepted May 13, 2010.

PART II: THE MAJORITY OF PATIENTS WITH ASYMPTOMATIC CAROTID DISEASE DO NOT REQUIRE INTERVENTION AND ARE BETTER TREATED MEDICALLY.

—Professor A. Ross Naylor

Thomas Kuhn invented the term "paradigm shift." This occurs when

> . . . scientists tend to work within one set of ideas about how the world is. Everything they do, be it experimental or theoretical, is informed by, and framed within, that set of ideas. However, there will be evidence that does not fit. At first, that evidence will be ignored or sabotaged. Eventually though, the anomalies will pile up so high that they simply cannot be ignored or sabotaged any longer. Then comes crisis.[1]

In this debate, I will contend that "anomalous" evidence challenges the "one-size-fits-all" approach to treating asymptomatic carotid disease. We need a paradigm shift in thinking.

In the 1970s, surgeons were convinced that carotid endarterectomy (CEA) prevented stroke in asymptomatic patients. Their intuition was vindicated with the Asymptomatic Carotid Atherosclerosis Study (ACAS)[2] and the Asymptomatic Carotid Surgery Trial (ACST),[3] leading the American Heart Association (AHA) to conclude that CEA was "recommended in highly selected patients with high-grade asymptomatic stenoses, provided it was performed by surgeons with <3% morbidity and mortality."[4] This is generally translated to mean,"CEA is appropriate in asymptomatic patients with 60% to 99% stenoses."

The AHA recommendation (updated in 2006)[4] is based on the highest level of evidence, so why the debate? Unlike the symptomatic trials, which provided level I evidence for intervention and enduring multidisciplinary consensus, there is less agreement about managing asymptomatic patients. Notwithstanding the conservatism of some neurologists, the only issue for many surgeons and interventionists is whether CEA or carotid artery stenting (CAS)

is now the preferred intervention. In their world, CEA significantly reduces the risk of stroke by 50%, and that (alone) is compelling enough evidence for intervening. Using Kuhn's principle, they are "working within one set of ideas about how the world is." They are also hostile to anyone who suggests that their reasoning might be flawed.

The AHA recommendation includes the phrase "highly-selected." Unfortunately, no clarification was forthcoming about what this meant, and physicians have to interpret this for themselves; in reality, it is ignored. However, defining who benefits most—and least—from intervention is crucial to this debate and brings us to those anomalies that challenge current guidelines and support a paradigm shift in thinking. These are chronologically listed in the Table, and the most important will be debated after reviewing how critics responded to them.

Physicians have (not unreasonably) adopted the role of patient advocate should anyone suggest that intervention might be unnecessary:

1. "You would never send someone home with occlusive disease of the left main coronary artery. Why then would you send home a patient with a critical stenosis of a dominant-hemisphere internal carotid with a 95% stenosis?"[34]
2. "It is politically untenable to deny women, and not men prophylactic CEA."[35]
3. "But what about the patient? He understands that his brain is threatened by a severe carotid stenosis, no matter what the overall percentage of this threat actually is. They should also understand that denying surgery equates to being exposed life-long to a cumulative risk of a cerebrovascular event."[36]

Vox populi comments include:

1. "As long as 80% of strokes are not preceded by a TIA, I will treat asymptomatic patients."
2. "Women live longer, therefore it is unreasonable to withhold CEA/CAS."
3. "Patients are not always compliant with taking medications. It is safer to offer CEA."
4. "Surgeons need to focus on the welfare of the individual and not the population."

Next comes media hype, a classic example being the 1994 *New York Times* commentary (after the ACAS Alert) which stated that "50% fewer strokes will occur if asymptomatic individuals with >60% stenoses are submitted to surgery."[37] This, I suspect, is a commonly quoted statistic when risk/benefit is discussed with patients. It is also a good example of being "economical with the actualité."

Methodologic criticisms include:

1. "As experts in this domain, we should rely on strong, though not necessarily fully evidence based arguments and draw our own conclusions about the case of our specific patient."[36]
2. "Subgroup analyses can be ignored as the trials were never powered to make these conclusions."
3. "These data are from very old studies and have little relevance in today's world, especially now that CAS is available."

Realities of professional life (conceded "off the record") include "if I do not operate on this patient, someone else will and I will lose income." Finally, if all else fails, why not resort to censure: (1) "why should we, who work in a first-world health service, pay any attention to someone working in a third-world system" (2005 Charing Cross Symposium), and (2) "what is more paradoxical is the attitude of some who become progressive opinion leaders, despite the fact that the message they deliver is a deliberate and insistent non-operating pleading in the case of asymptomatic disease. Using mostly statistical or economic arguments, rather than medical evidence, they aim to demonstrate that prophylactic CEA, even in being probably the safest approach in skilled hands, was not medically justified, nor cost-effective for public savings."[36] Ouch!

The preceding counterarguments to the anomalies in the Table mask a growing crisis, primarily because some are now too important to remain ignored:

First, ACAS/ACST showed that almost 90% of medically treated patients were never destined to suffer a stroke ≤5 years.[2,3] That should, of course, make me the winner in this debate (read the title), but I see you remain unconvinced.

Second, is the uncomfortable observation that even if you could treat everyone fulfilling ACAS criteria with a 2.3% procedural risk, 95% of strokes will still happen.[6,29] This is because CEA/CAS cannot prevent the 70% of strokes unrelated to carotid disease, while two-thirds of patients with carotid origin strokes will not have significant stenoses and 15% to 20% will present with a TIA. That leaves about 8 to 10 patients whose strokes will be attributable to significant, asymptomatic carotid disease in whom to target interventions. However, CEA reduces stroke by 50%, so that only five strokes (at most) will be prevented. Consider that the next time someone justifies mass intervention because "80% of strokes are unheralded."

If you still believe that CEA/CAS confers benefit in most asymptomatic patients, have you considered the logistics of finding and treating them? With a population of 1.3 million in Hawaii, let us assume that Peter Schneider and his colleagues can somehow identify the 1% of Hawaiians (13,000) with an asymptomatic 60% to 99% stenosis (this would normally take years). Assuming theater/catheter suites work every weekday (260 per annum) and 10 CEA/CAS procedures are performed somewhere on the island on *every* one of these days (ie, 2600 interventions in asymptomatic patients per year; quite a big task), it would take 5 years to clear the backlog. During this time, some will suffer a stroke whilst awaiting treatment and more "at-risk" populations will emerge. In reality, a policy of operating on as many asymptomatic patients as possible will only prevent about 1% of all strokes.

But mass interventions consume resources. Using ACAS data, performing CEA/CAS with a 2.3% risk pre-

Table. Anomalies regarding a "one-size-fits-all" policy of offering carotid endarterectomy *(CEA)* or carotid artery stenting *(CAS)* to "standard-risk" patients with 60% to 99% asymptomatic carotid stenoses

1991	ACAS: 40% of surgeon applicants rejected, raising questions about generalizability[5]
1995	ACAS: With a 2.3% procedural risk, CEA prevents only 59 strokes at 5 years per 1000 CEAs[2]
	ACAS: With procedural risk included, CEA conferred no benefit in women[2]
	ACAS: No relationship between stenosis severity/bilateral disease and late stroke risk[2]
	Even if you could treat every patient, 95% of all strokes in the community will still occur[6]
1996	Hertzer concedes that the annual risk of stroke in ACAS was much lower than expected[7]
	ACAS: Even with the procedural risk excluded, CEA still conferred no benefit in women[8]
	First editorial to question whether ACAS results warrant a tenfold increase in CEA numbers[9]
1997	Canadian Neurologists & Stroke Physicians recommend against CEA and screening[10]
2000	ACAS: CEA does not confer significant benefit in patients with a contralateral occlusion[11]
	Fifty-five percent of late strokes are cardioembolic or lacunar (ie, majority are not due to internal carotid artery embolism)[12]
2001	Seven of 10 states in USA report procedural risks >3% after CEA[13]
	Using ACST entry criteria, the average procedural risk after CEA in 10 US states was 5.9%[13]
2002	ACAS: Had their data been analyzed at 4 years, CEA would have conferred no benefit[9]
2003	European Stroke Initiative suggests that medical treatment is now probably the best option[14]
	Editorial suggests that the randomized trials should be repeated[15]
2004	ACST: CEA conferred no benefit in patients aged >75 years[3]
	ACST: No association between stenosis severity/bilateral disease and late stroke risk[3]
	ACST: If procedural risk included, CEA conferred no significant benefit in women[16]
	ACST: Most of the benefit was seen in patients with a prerandomization cholesterol >6.5[3]
	Using ACST inclusion criteria, the average procedural risk after CEA in 10 US states was 5.4%[17]
	Meta-analysis of 46 contemporary surgical studies found mortality 8 times higher and death/stroke 3 times higher compared with outcomes in ACAS[18]
2005	Ninety-two percent of all carotid revascularizations in USA are now performed in asymptomatic patients[19]
2007	US Task Force recommends against screening (benefits too low and do not outweigh risks)[20]
	Annual risk of stroke in medically treated patients has been decreasing over the last 20 years[21]
2008	Published evidence that high statin therapy stabilizes asymptomatic carotid plaques[22]
	Even with 15-year follow-up, it is never cost-effective to offer CEA to females, irrespective of age[23]
	New England Journal of Medicine poll: 50% of respondents worldwide would treat asymptomatic patients conservatively[24]
	Editorial suggests that it may be time to stop intervening in asymptomatic patients[25]
	If the procedural risk of death/disabling stroke was >2.1%, or if the annual rate of fatal/disabling stroke was <1.09%, CEA/CAS will not confer any long-term benefit[26]
2009	Systematic review: Noninterventional therapy now safer than CEA/CAS (attributed to improvements in medical therapy) and is 3 to 8 times more cost-effective[27]
	94% of CEA/CAS procedures in the US are ultimately unnecessary, costing $2.1 billion per annum[28,29]
	Evidence of sustained decline in annual stroke risk in medically treated patients in ACAS and ACST[28]
2010	Evidence that high statin therapy significantly reduces spontaneous embolization[30]
	Meta-analysis of 3 recent studies (1635 patients); ipsilateral stroke risk now only 0.5% per year[31]
	More calls for randomized trials comparing CEA with CAS to include a third medical limb[28,32,33]

ACAS, Asymptomatic Carotid Atherosclerosis Study; *ACST,* Asymptomatic Carotid Surgery Trial.

vents 59 ipsilateral strokes/1000 procedures at 5 years[38] (indisputable fact). The number of "any" strokes prevented = 51. In 2005, 122,986 revascularizations were undertaken in asymptomatic patients in the United States of America (USA),[19] and simple calculation (59 × 122.986) shows that ipsilateral strokes will be prevented in only 7256 patients. This also means that in 2005, 115,730 (94%) underwent an ultimately unnecessary intervention. Using USA financial data,[19] unnecessary interventions cost USA health providers $2.1 billion each year.[28,29] That is surely unsustainable.

Ah, but you probably feel that my debate has focussed excessively on logistics, cold statistics, and expenditure, and not enough on the individual patient? No, I would not allow that. Notwithstanding the 30-plus anomalies detailed in the Table, the single most important reason why a paradigm shift in thinking is unavoidable is because the most venerated of "sacred cows" is now under threat. That is the basic assumption that the annual rate of stroke in medically treated patients remains about 2%. If the annual risk has decreased since ACAS/ACST results were published, many of the risk/benefit calculations become vulnerable to challenge. If the annual risk falls to 1%, it is unlikely that CEA/CAS could ever confer significant benefit.[27] What would you think if I suggested that the annual risk of ipsilateral stroke may now be as low as 0.5% to 0.7%?

Abbott was one of the first to observe that the annual risk of stroke in medically treated patients has declined significantly during last 20 years,[21,25,27] and her latest meta-analysis concludes that noninterventional therapy is the safer option, while also being more cost-effective.[26] A second (smaller) meta-analysis published in 2010 included natural history data from three studies recruiting after 2000 and found that the average annual risk of ipsilateral stroke in 1635 medically treated patients was 0.5%.[30] Abbott (and others) have attributed this decline in stroke risk to improvements in BMT, especially through the use of high-dose statins.[21,25,27,28,33] Not surprisingly, this has elicited

the inevitable counterargument[39] (recognize a trend?), primarily because some studies in Abbott's meta-analysis included patients with stenoses of 50% to 99% as opposed to 60% to 99%. However, neither ACAS/ACST nor a raft of natural history studies have consistently shown that late stroke is associated with stenosis severity.[2,3,28] Moreover, an alternative interpretation of data from ACAS and ACST suggests that they, too, have encountered year-on-year reductions in stroke risk. They just haven't acknowledged it yet. ACAS published 5-year data in 1995, ACST in 2004, and then released 6- to 10-year data during 2008 and 2009,[2,3,28] giving observers three sequential 5-year periods for comparison. In 1995, ACAS reported a 5-year risk of any stroke of 17.5% (ie, 3.5% per annum) in medically treated patients. The risk of any stroke in years 1 to 5 of ACST fell to 11.8% (ie, 2.4% per annum), whereas in years 6 to 10, the second 5-year period of study, the risk of any stroke decreased to 7.2% (ie, 1.4% per annum). In 1995, ACAS reported a 5-year risk of ipsilateral stroke of 11.0% (ie, 2.2% per annum) in medically treated patients. By 2004, the 5-year risk of ipsilateral stroke in ACST had fallen to 5.3% (ie, 1.1% per annum), whereas in the second five-year period (years 6-10 of ACST), the risk of ipsilateral stroke decreased to 3.6% (ie, 0.7% per annum). This means that the average annual risk of any stroke has declined by 60%, from 3.5% to 1.4%, in the 15 years since ACAS published, whereas the annual average risk of ipsilateral stroke has declined by 67% from 2.2% to 0.7%. This, in conjunction with Abbott's meta-analysis, suggests that there has been a significant, sustained decrease in the annual risk of stroke.

So who will win this debate? The paradox is that I can neither win nor lose. Until influential bodies (ie, the AHA) consider the implications of a declining stroke risk and revise their recommendation (ie, triggering a paradigm shift in thinking), nothing will change. This is because the AHA wields the greatest influence over practice worldwide and surgeons and interventionists will continue to offer mass interventions, not least to minimize medicolegal censure. To many observers,[28,32,33] including the principle investigator of CREST,[32] we need to undertake an adequately powered randomized trial that includes treatment arms for CEA, CAS, and BMT. This should make it possible to test algorithms for identifying "high-risk for stroke" subgroups, for example, TCD embolization, silent infarction on CT, incomplete circle of Willis, computerized plaque morphology, and biomarkers. Surely we must focus resources toward intervening in only a very small cohort of "high-risk for stroke" patients?

Conversely, it is also true that I cannot lose this debate. It is indisputable that the vast majority of patients with asymptomatic carotid disease will never suffer a stroke; only 1% of strokes will be prevented through a mass campaign of uncritical intervention, 94% of interventions in asymptomatic patients are ultimately unnecessary, and the annual risk of stroke is now very much lower than it was in 1995. How else could you interpret the data? Unless, of course, you remain distracted by other conflicts of interest . . . .

REFERENCES

1. Brooks M. Prologue. Thirteen things that don't make sense. London: Profile Books Ltd; 2010. p. 3-4.
2. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-8.
3. Asymptomatic Carotid Surgery Trial Collaborators. The MRC Asymptomatic Carotid Surgery Trial (ACST): carotid endarterectomy prevents disabling and fatal carotid territory strokes. Lancet 2004;363:1491-502.
4. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, et al. Primary prevention of ischemic stroke. A guideline from the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Stroke 2006;37:1583-663.
5. Moore WS, Young B, Baker WH, Robertson JT, Toole JF, Vescera C, Howard VJ. Surgical results: a justification of the surgeon selection process for the ACAS trial. The ACAS investigators. J Vasc Surg 1996;23:323-8.
6. Hankey GJ. Asymptomatic carotid stenosis: how should it be managed? Med J Aust 1995;163:197-200.
7. Hertzer NR. A personal view: the Asymptomatic Carotid Atherosclerosis Study results—read the label carefully. J Vasc Surg 1996 23: 167-71.
8. Young B, Moore WS, Robertson JT, Toole JF, Ernst CB, Cohen SN, et al. An analysis of peri-operative surgical mortality and morbidity in the Asymptomatic Carotid Atherosclerosis Study. Stroke 1996;27: 2216-24.
9. Barnett HJM, Eliasziw M, Meldrum HE, Taylor DW. Do the facts and figures warrant a tenfold increase in the performance of carotid endarterectomy on asymptomatic patients? Neurology 1996;46:603-8.
10. Perry JR, Szalai JP, Norris JW. Consensus against both endarterectomy and routine screening for asymptomatic carotid artery stenosis: the Canadian Stroke Consortium. Arch Neurol 1997;54:25-8.
11. Baker WH, Howard VJ, Howard G, Toole JF, for the ACAS Investigators. Effect of contralateral occlusion on long term efficacy of endarterectomy in the asymptomatic Carotid Atherosclerosis Study. Stroke 2000;31:2330-4.
12. Inzitari D, Eliasziw M, Gates P, Sharpe BL, Chan RK, Meldrum HE. The causes and risk of stroke patients with asymptomatic internal carotid artery stenosis. NEJM 2000;342:1693-700.
13. Kresowik TF, Bratzler DW, Karp HR, Hemann RA, Hendel ME, Kresowik RA, et al. Multistate utilization processes and outcomes of carotid endarterectomy. J Vasc Surg 2001;33:227-35.
14. The European Stroke Initiative Executive Committee and the EUSI Writing Committee. European Stroke Initiative Recommendations for stroke management—Update 2003. Cerebrovasc Dis 2003;16: 311-37.
15. Chaturvedi S. Should the multicenter carotid endarterectomy trials be repeated? Arch Neurol 2003;60:774-5.
16. Rothwell PM. ACST: Which subgroups will benefit most from carotid endarterectomy? Lancet 2004;364:1122-3.
17. Bunch CT, Kresowik TF. Can randomized trial outcomes for carotid endarterectomy be achieved in community wide practice? Semin Vasc Surg 2004;17:209-13.
18. Rothwell PM, Goldstein LB. Carotid endarterectomy for asymptomatic carotid stenosis: Asymptomatic Carotid Surgery Trial. Stroke 2004;5: 2425-7.
19. McPhee JT, Schanzer A, Messina LM, Eslami MH. Carotid artery stenting has increased rates of post-procedure stroke, death and resource utilization than does carotid endarterectomy in the United States, 2005. J Vasc Surg 2008;48:1442-50, 1450.e1.
20. US Preventive Services Task Force. Screening for carotid artery stenosis: US Preventive Services Task Force Recommendation Statement. Ann Int Med 2007;147:854-9.
21. Abbott AL, Bladin CF, Levi CR, Chambers BR. What should we do with asymptomatic carotid stenosis? Int J Stroke 2007;2:27-39.

22. Kadoglou NP, Gerasimidis T, Moumtzouoglou A, Kapelouzou A, Sailer N, Fotiadis G, et al. Intensive lipid-lowering therapy ameliorates novel calcification markers and GSM score in patients with carotid stenosis. Eur J Vasc Endovasc Surg 2008;35:661-8.
23. Henriksson M, Lundgren F, Carlsson P. Cost-effectiveness of endarterectomy in patients with asymptomatic carotid artery stenosis. Br J Surg 2008;95:715-20.
24. New England Journal of Medicine. Clinical decisions interactive feature. http://www.nejm.org/clinical%2Ddecisions/20080410/#commentbox.
25. Abbott A. Asymptomatic carotid artery stenosis: it's time to stop operating. Nature Clin Pract Neurol 2008;4:4-5.
26. Arazi HC, Capparelli FJ, Linetzky B, Rebolledo FP, Augustovski F, Wainsztein NA. Carotid endarterectomy in asymptomatic stenosis: a decision analysis. Clin Neurol Neurosurg 2008;110:472-9.
27. Abbott AL. Medical (non-surgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. Stroke 2009;40:e573-83.
28. Naylor AR, Gaines PA, Rothwell PM. Who benefits most from intervention for asymptomatic carotid stenosis: Patients of professional? Eur J Vasc Endovasc Surg 2009;37:625-32.
29. Naylor AR, Gaines PA, Rothwell PM. Corrigendum to: who benefits most from intervention for asymptomatic carotid stenosis: patients of professional? Eur J Vasc Endovasc Surg 2009;37:625-632; Eur J Vasc Endovasc Surg 2009;38:657.
30. Spence DJ, Coates V, Li H, Tamayo A, Munoz C, Hackam DG, et al. Effects of intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis. Arch Neurol 2010;67:180-6.
31. Rothwell PM. Carotid stenting: more risky than endarterectomy and often no better than medical treatment alone. Lancet 2010;375:957-9.
32. Brott T. Asymptomatic carotid disease: where do we go from here? Vasc News Jan 2010:4-6.
33. Veith FJ, Andros G. TACIT must be funded: we must pay now or pay later. http://www.vascularweb.org/professionals/vascular_specialist/vol5/number8/newspaper_4_56642_57060.html.
34. Wholey MH, Barbato JE. Is carotid stenting justified in the asymptomatic patient? Perspectives on indications for CAS. Cath Cardiovasc Interv 2007;69:1081-3.
35. Moneta G. Commentary. J Vasc Surg 2008;48:769-70.
36. Chiche L, Goulfier C. Best practice for asymptomatic carotid disease. In: Jacobs M, editor. Best practice in vascular procedures. Turin: Minerva Medica; 2010. p. 21-36.
37. Altman LK. Surgery is found to fight stroke. NY Times, Oct 1, 1994.
38. Naylor AR. What is the current status of angioplasty vs endarterectomy in patients with asymptomatic carotid artery disease? Journal of Cardiovascular Surgery 2007;48:161-180.
39. Kahn J. Medical therapy alone best for asymptomatic severe carotid disease? http://www.tctmd.com/show.aspx?id=80590. Accessed Dec 8, 2009.

Submitted May 12, 2010; accepted May 13, 2010.

COMMENTARY

Thomas L. Forbes, MD, *London, Ontario, Canada*

Dr Schneider and Prof Naylor have offered a spirited debate regarding the optimal approach to patients with significant asymptomatic carotid artery stenoses. Their arguments are clear, reasoned, passionate, and in direct opposition with each other. Both would agree that stroke in patients with asymptomatic stenoses is a relatively rare event, and, given its potentially devastating consequences, should be avoided. Further points of agreement are few and far between.

Most issues of contention are a result of differing interpretations of the same data or studies. For example, Prof Naylor's claim that stroke risk is declining with medical therapy is supported by several studies with which Dr Schneider has issue given their inclusion of patients with lesser degrees of stenosis who would not have been surgical candidates in the first place. Prof Naylor counters with the argument that stroke risk has not been consistently shown to be directly related to degree of stenosis anyway. Such differences are probably irreconcilable.

In any event, strategies consisting of medical therapy alone or combined with surgical intervention have both proven highly successful at preventing stroke in asymptomatic patients. Innumerable studies offer support, and few would argue with this. Where controversy remains, and will probably always persist, is in which instances should one strategy be chosen over another? Our debaters both recommend another study to help to answer these questions, but I suspect that such a study's data would continue to be interpreted differently depending on what side of the argument one sits. This likely will remain a polarizing issue.

So, although convincing, Dr Schneider and Prof Naylor have probably not succeeded in persuading each other to change their approaches, but have certainly gone a long way in educating the rest of us.